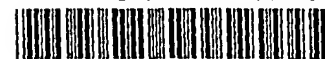


translation

PATENT COOPERATION TREATY

PCT/EP2003/009451



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference M/43126-PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP2003/009451	International filing date (day/month/year) 26 August 2003 (26.08.2003)	Priority date (day/month/year) 27 August 2002 (27.08.2002)
International Patent Classification (IPC) or national classification and IPC C12P 13/04		
Applicant BASF AKTIENGESELLSCHAFT		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>9</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of _____ sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input checked="" type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>

Date of submission of the demand 24 March 2004 (24.03.2004)	Date of completion of this report 09 December 2004 (09.12.2004)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2003/009451

## I. Basis of the report

### 1. With regard to the elements of the international application:\*

☐ the international application as originally filed

☒ the description:

pages 1-38, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

☒ the claims:

pages 4(Part), 5-16, as originally filed  
pages 1-3, 4(Part), as amended (together with any statement under Article 19  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

☒ the drawings:

pages 1/3-3/3, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

☐ the sequence listing part of the description:

pages \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

### 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

### 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

### 4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages \_\_\_\_\_

☐ the claims, Nos. \_\_\_\_\_

☐ the drawings, sheets/fig \_\_\_\_\_

### 5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2003/009451

## IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

See Supplemental Sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. \_\_\_\_\_

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 03/09451

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV.3

**Lack of unity of invention**

This Authority has determined that this international application contains multiple inventions or groups of inventions which are not linked by a single general inventive concept (PCT Rule 13.1), as follows:

I: claims 1 to 14 and 16;

II: claim 15.

The reasons for this are the following:

**Invention I** addresses the problem of providing a method of producing by fermentation a sulfur-containing fine chemical (L-methionine), this problem being solved by the use of a coryneform bacterial culture in which at least one heterologous nucleotide sequence that codes for a protein with methylenetetrahydrofolate reductase (metF) activity is expressed.

**Invention II** addresses the problem of providing an L-methionine-containing animal feed additive from fermentation broths. This problem is solved by cultivating and fermenting any L-methionine-producing microorganism, removing water and biomass and drying the resultant fermentation broth. Invention II does not make reference to invention I.

Since inventions I and II solve different problems, the solutions to these problems are also different and not linked by a single common inventive concept.

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV.3

The special technical features which the respective inventions contribute to the prior art (use of a specific microorganism in invention I; preparing a fermentation broth of any microorganism in invention II) are also different and therefore lack unity.

In light of the brevity of the PCT proceedings and owing to the fact that the additional search and substantive examination did not require a large amount of additional work and since claim 15 does not appear to be novel anyway (see Box V), the applicant has not been requested to pay an additional fee during the international proceedings.

However, this point will come up for discussion in the regional proceedings before the EPO.

Furthermore, the last paragraph in Box V, point 5), should be noted with regard to unity of invention.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 03/09451

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims	4	YES
	Claims	1-3, 5-16	NO
Inventive step (IS)	Claims		YES
	Claims	1-16	NO
Industrial applicability (IA)	Claims	1-16	YES
	Claims		NO

**2. Citations and explanations**

1). The international search report citations are listed below with the following abbreviations:

D1: WO 02/10206 (DEGUSSA) 7 February 2002 (2002-02-07)

D2: WO 93/17112 A (GENENCOR INT) 2 September 1993 (1993-09-02)

D3: KRAMER R: "Genetic and physiological approaches for the production of amino acids" JOURNAL OF BIOTECHNOLOGY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 45, no. 1, 12 February 1996 (1996-02-12), pages 1-21, XP004036833 ISSN: 0168-1656.

2). The present application:

Claims 1 to 14 of the present application relate to a method of producing by fermentation a sulfur-containing fine chemical (L-methionine), in which method a coryneform bacterial culture is used in which at least one heterologous nucleotide sequence that codes for a protein with methylenetetrahydrofolate reductase (metF) activity is expressed.

Claim 15 relates to a method of producing an L-methionine-containing animal feed additive from fermentation broths by cultivating and fermenting any L-methionine-producing microorganism, removing water and biomass and drying the resultant fermentation broth.

Claim 16 uses the microorganisms used in the method of claims 1 to 14, and claim 16 is therefore regarded as a multiple step method that incorporates claims 1 to 14.

The present application contains the following defects, which are critical for the substantive examination (PCT Articles 5 and 6):

-) The term "sulfur-containing" in the claims (in particular claim 1) and in the description is so broad and undefined that it makes the scope of the claims unclear. Furthermore, it is clear from the description and the examples that only L-methionine is produced.

-) The feature "less than 100% sequence homology" in claim 3 is meaningless because all sequences other than the metF-coding sequences from *Corynebacterium glutamicum* ATCC 13032 are covered by the scope of the claim. This claim is therefore too broad, vague and undefined and is interpreted in its broadest form for the purpose of the substantive examination.

-) Claims 5 and 6 contain so-called "functional definitions", i.e. a feature is defined by its function or the result to be achieved by means of this feature. In the present case, this objection refers to the "homologous sequences", which are only

defined by their function and therefore require an unreasonable amount of work on the part of the user of the patent in testing the functions.

The same objection is also made against claims 10 to 12, in which this type of functional feature "and mutated in such a way that" makes the scope of the claims entirely vague and undefined.

Claims 5, 6 and 10 to 12 are therefore vague and undefined and, in light of the description, much too broad.

Since the term "homologous" *per se* is not defined, claims 5 and 6 were also examined in their broadest definition.

3). Brief discussion of the prior art documents:

D1 describes the production of methionine using microorganisms, wherein *inter alia* also the metF gene is (over)expressed (see, for example, claim 9 in D1). Since the gene (preferably from *C. glutamicum* 13032) used in D1 can also have sequence variation (see, for example, claims 1 to 5 in D1), D1 is also relevant for the present claims, which relate to a(n) (unspecific) sequence homology.

Moreover, D1 discloses methods for producing an L-methionine-containing feed additive from fermentation broths which include the same steps as the present claim 15 (see D1, page 19). D1 is therefore prejudicial to the novelty of claims 1 to 3 and 5 to 16 according to the application and relevant for the assessment of inventive step for claims 1 to 16.



D2 relates to the biosynthetic production of amino acids in microorganisms.

D3 is a background document concerning the metabolic pathways in biosynthetic amino acid production.

4). Novelty (PCT Article 33(1) and (2)):

As already mentioned in point 3), the subject matter of claims 1 to 3 and 5 to 16 is not novel in light of D1.

5). Inventive step (PCT Article 33(1) and (3)):

Although claim 4 is novel insofar as it does not include any unspecific sequence homologies, an inventive step cannot be recognized.

The present application and the prior art differ by the selection of the microorganisms listed in claim 4. It is not clear what problem is solved by these microorganisms in relation to the methods known from the prior art.

The applicant is again reminded that the use of transgenic bacteria which contain a heterologous nucleotide sequence that codes for a protein with methylenetetrahydrofolate reductase (metF) activity is known in the production of methionine (see D1). Although the bacterial strains listed in claim 4 are not mentioned in the aforementioned documents, said bacterial strains are apparently known for having methylenetetrahydrofolate reductase (metF) activity (see description, for example, pages 12-14 of the present application). It is therefore not clear what advantage there is in using said microorganisms over

those from the prior art.

The results of a comparative test disclosed on page 38 of the present description show only that the microorganism transformed by the metF gene has higher activity. This, however, is already known from the prior art (see page 28 in D1).

An inventive step therefore cannot be recognized for the subject matter of claim 4.

It should also be noted, as a precaution, that if an inventive step were to be recognized in the selection of these specific microorganisms, the selection of the individual microorganisms would constitute an invention in each case, and claim 4 would therefore break down into 26 different inventions and would therefore lack unity.

6). Industrial applicability (PCT Article 33(1) and (4)):

The subject matter of claims 1 to 16 is industrially applicable.